

**Remarks**

The Office Action mailed 21 April 2004 has been received and reviewed. Claims 1, 4, 21, 24, 47, 50, 54, 77, 81, 90 and 91 having been amended; claims 34, 35, 57 and 58 having been canceled; and claims 92-101 having been added; the pending claims are claims 1, 3-13, 21, 23, 24, 33, 36, 37, 41-47, 49-56, 59-69, 72, 73, 75-81, and 90-101. Reconsideration and withdrawal of the rejections are respectfully requested.

**Status of Claims**

Applicants request correction of the Examiner's statement of the disposition of the claims in the Office Action Summary mailed 21 April 2004.

With respect to pending claims, claim listing in Applicant's Response mailed December 19, 2003, indicates that claims 1, 3-13, 21, 23, 24, 33-37, 41-47, 49-69, 72, 73, 75-81, 90 and 91 were pending (claims 2, 14-20, 22, 25-32, 38-40, 48, 70, 71, 74 and 82-89 being canceled). Thus, the pending claims listed in the Office Action Summary should include only claims 1, 3-13, 21, 23, 24, 33-37, 41-47, 49-69, 72, 73, 75-81, 90 and 91. Applicants apologize for any conflicting statements in the body of the Response.

With respect to rejected claims, although the list of rejected claims in the Office Action Summary mailed 21 April 2004 includes claims 69, 72, 73, 75, 76, and 78-80, these claims were not rejected in the body of the Office Action. It appears that claims 72, 73, 75, 76 and 78-80 were allowable in view of the rejections, and that claim 69 would have been allowable if rewritten as an independent claim. Accordingly, claim 69 has been rewritten as an independent claim, although the limitation concerning Western blot detection has been deleted, and the claim recites "an antibody" instead of a "monoclonal" antibody as in claim 47, from which it depended. Clarification of the status of claims 69, 72, 73, 75, 76, and 78-80, and notification of their allowability, is respectfully requested.

In view of the uncertainties regarding disposition of the claims in the Office Action mailed 21 April 2004, if any of the claims are not allowable in their present form, Applicants

request that the Examiner issue a second, non-final Office Action to allow the Applicants a full and fair opportunity to respond to the claim rejections.

**Rejection under 35 U.S.C. §112, Second Paragraph**

The Examiner rejected claims 4, 50, 54, 77, and 81 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner indicated that the use of the laboratory designations D7 and B2D6 renders the claims indefinite. This rejection is respectfully traversed.

In accordance with the suggestion of the Examiner, claims 4, 50, 54, 77 and 81 have been amended to recite the depository accession number of the hybridomas. It is submitted that this amendment obviates the rejection of claims 4, 50, 54, 77, and 81 under 35 U.S.C. §112, second paragraph.

The Examiner also stated that it is unclear how claim 24 further limits claim 21. This rejection is also respectfully traversed. However, in order to clarify the invention, claim 24 has been amended to recite that the method of claim 21 further comprises, prior to the detecting step, the step of fixing the cells on a slide, wherein the detecting step comprises detecting the reagent-nucleic acid binding using immunofluorescence staining. It is submitted that the amendment to claim 24 obviates the rejection under 35 U.S.C. §112, second paragraph.

The Examiner also stated that the metes and bounds of claim 91 are unclear. Applicants disagree. Claim 90 recites that changes in EphA2 expression level, intracellular localization pattern or phosphorylation content can indicate the presence of cancer cells in selected cell population. Claim 91 recites that these changes may be indicative of the presence of nonmetastatic cancer cells in the cell population.

Metastatic, nonmetastatic and normal cells are mutually distinguishable according to the invention using one or more of the recited changes in EphA2 expression level, localization pattern or phosphorylation content. The Examiner is incorrect in stating that the art teaches that normal cells do not express, or express very low levels of, EphA2, and thus are not

distinguishable from non-metastatic cancer cells. Normal cells do express detectable levels of EphA2. See, for example, at page 5, line 9 and page 7, line 21, of the specification, which state that in normal breast epithelial cells, EphA2 is expressed. Nonmetastatic cancer cells (claim 91) can be distinguished from normal cells because nonmetastatic cancer cells have a lower level of EphA2 expression than normal cells. See, e.g., specification at page 5, lines 10-11 and page 7, lines 23-25. Applicant submits that the metes and bounds of claim 91, which further characterizes the "cancer cell" recited in claim 90 as a "metastatic" cancer cell, are accordingly discernable.

Reconsideration and withdrawal of the rejections of claims 4, 21, 50, 54, 77, 81 and 91 under 35 U.S.C. §112, second paragraph, is respectfully requested.

**Rejection under 35 U.S.C. §112, First Paragraph**

The Examiner rejected claims 4, 50, 54, 77 and 81 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner notes that the Declaration regarding deposit of the hybridoma cell lines D7 and B2D6, but that the Declaration is directed to U.S. Ser. No. 09/640,935 instead of the instant U.S. Ser. No. 09/640,952. This rejection is respectfully traversed.

Applicants submit that the Declaration submitted March 24, 2003, a copy of which is attached, is properly directed to the instant U.S. Ser. No. 09/640,952. It is respectfully submitted that this Declaration obviates rejection of claims 4, 50, 54, 77 and 81 under 35 U.S.C. §112, first paragraph. Reconsideration and withdrawal of the rejection is respectfully requested.

**Rejection under 35 U.S.C. §102(b)**

The Examiner rejected claims 21, 23, 90 and 91 under 35 U.S.C. §102(b) as being anticipated by Easty et al. (International Journal of Cancer, 1995;60:129-136) as evidenced by

the abstract of Chen et al. (Journal of Biological Chemistry 1998;273:24670-24675). This rejection is respectfully traversed.

Claim 21 has been amended to recite that the tissue sample comprises cancer cells selected from the group consisting of breast cancer cells, kidney cancer cells, prostate cancer cells, lung cancer cells, colon cancer cells and epithelial cancer cells. Easty et al. does not describe detection of nucleic acid coding for the EphA2 protein in breast cancer cells, kidney cancer cells, prostate cancer cells, lung cancer cells, colon cancer cells or epithelial cancer cells. Easty et al. thus does not anticipate claim 21 and claim 23, which depends therefrom, at least because it does not teach each element of the claimed invention.

Claim 90 has been amended to clarify that the monoclonal antibody used to detect the cell specifically binds EphA2. Easty et al. describes polyclonal serum that binds EphA2, but does not teach an anti-EphA2 monoclonal antibody. Easty et al. thus does not anticipate claim 90 and claim 91, which depends therefrom, at least because it does not teach each element of the claimed invention.

Reconsideration and withdrawal of the rejection of claims 21, 23, 90 and 91 under 35 U.S.C. §102(b) as being anticipated by Easty et al. as evidenced by the abstract of Chen et al. is respectfully requested.

#### **Rejection 35 U.S.C. §103(a)**

The Examiner rejected claims 1, 3, 5, 11, 33, 34, 35, 41, 47, 49, 55, 56, 57, 58, 61, 64 and 68 under 35 U.S.C. §103(a) as being unpatentable over Easty et al. (International Journal of Cancer 1995;60:129-136) as evidenced by the abstract of Chen et al. (Journal of Biological Chemistry 1998;273:24670-24675) and Lindberg et al. (Molecular and Cellular Biology 1990;10:6316-6324) in view of Larrick et al. (In: Human Hybridomas and Monoclonal Antibodies, Engleman and Foug, Eds. 1985;8-9).

The Examiner rejected claims 1, 3, 5, 9-11, 33, 34, 35, 41, 43-45, 47, 49, 55, 56, 57, 58, 61, 64, and 66-68 under 35 U.S.C. 103(a) as being unpatentable over Easty et al. (*International Journal of Cancer* 1995;60:129-136) as evidenced by the abstract of Chen et al. (Journal of

Biological Chemistry 1998;273:24670-24675) and Lindberg et al. (Molecular and Cellular Biology 1990;10:6316-6324) in view of Larrick et al. (In: Human Hybridomas and Monoclonal Antibodies, Engleman and Fount, Eds., 1985, 8-9.) And applied to claims 1, 3, 5, 11, 33, 34, 35, 41, 45, 47, 49, 55, 56, 57, 58, 61, 64 and 68 above, and further in view of the abstract of Muhlbauer et al. (Clinical Cancer Research, 1999;5:1099-1105).

The Examiner rejected claims 1, 3, 5, 11, 12, 33, 34, 35, 41, 45, 46, 47, 49, 55, 56, 57, 58, 61, 64 and 68 under 35 U.S.C. 103(a) as being unpatentable over Easty et al. (International Journal of Cancer, 1995;60:129-136) as evidenced by the abstract of Chen et al. (Journal of Biological Chemistry, 1998;273:24670-24675) and Lindberg et al. (Molecular and Cellular Biology 1990;10:6316-6324) in view of Larrick et al. (In: Human Hybridomas and Monoclonal Antibodies, Engleman and Fount, Eds. 1985, pp. 8-9.) as applied to claims 1, 3, 5, 11, 33, 34, 35, 41, 45, 47, 49, 55, 56, 57, 58, 61, 64 and 68 above and further in view of Easty et al. (International Journal of Cancer, 1997;71:1061-1065).

The Examiner rejected claims 1, 3, 5, 6, 7, 11, 33, 34, 35, 41, 45, 47, 49, 55, 56, 57, 58, 61, 64, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Easty et al. (International Journal of Cancer 1995;60:129-136) and the abstract of Chen et al. (Journal of Biological Chemistry 1998;273:24670-24675) and Lindberg et al. (Molecular and Cellular Biology 1990;10:6316-6324) and Larrick et al. (In: Human Hybridomas and Monoclonal Antibodies, Engleman and Fount, Eds., 1985, pp. 8-9) as applied to claims 1, 3, 5, 11, 33, 34, 35, 41, 45, 47, 49, 55, 56, 57, 58, 61, 64, and 68 above, and further in view of Kerr and Thorpe (LabFac Immunochemistry, 1994; page 115 and 157).

The Examiner rejected claims 1, 3, 5, 11, 33, 34, 35, 41, 45, 47, 49, 51-53, 55, 56, 57, 58, 61, 64 and 68 under 35 U.S.C. 103(a) as being unpatentable over Easty et al. (International Journal of Cancer, 1995;60:129-136) and the abstract of Chen et al. (Journal of Biological Chemistry, 1998;273:24670-24675) and Lindberg et al. (Molecular and Cellular Biology, 1990;10:6316-6324) and Larrick et al. (In: Human Hybridomas and Monoclonal Antibodies, Engleman and Fount, Eds., 1985, pp. 8-9) as applied to claims 1, 3, 5, 11, 33, 34, 35, 41, 45, 47,

49, 55, 56, 57, 58, 61, 64 and 68 above, and further in view of Kerr and Thorpe (Immunochemistry LabFax, 1994, 191-197).

The rejection of the above-identified claims 1, 3, 5-7, 9-12, 33-35, 41, 43-47, 49, 51-53, 55-58, 61, 64, and 66-68 under 35 U.S.C. 103(a) is respectfully traversed.

Applicants note that claims 8, 13, 36, 37, 42, 59, 60, 62, 63, and 65 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 1 has been amended to include the limitations of claims 36 and 37 (cells selected from the group consisting of breast cancer cells, kidney cancer cells, prostate cancer cells, lung cancer cells, colon cancer cells and epithelial cancer cells) and claim 47 has been amended to include the limitations of claims 59 and 60 (cells selected from the group consisting of breast cancer cells, kidney cancer cells, prostate cancer cells, lung cancer cells, colon cancer cells and epithelial cancer cells). It is respectfully submitted that these amendments render moot the rejection of claims 1 and 47, as well as claims dependent therefrom (namely, claims 1, 3, 5-7, 9-12, 33-35, 41, and 43-46 which depend from claim 1; and claims 49, 51-53, 55-58, 61, 64, and 66-68 which depend from claim 47).

Reconsideration and withdrawal of the rejection of claims 1, 3, 5-7, 9-12, 33-35, 41, 43-47, 49, 51-53, 55-58, 61, 64, and 66-68 under 35 U.S.C. 103(a) in view of the references cited above is respectfully requested.

**Amendment and Response**

Page 20 of 20

Serial No.: 09/640,952

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For: EPHA2 AS A DIAGNOSTIC TARGET FOR METASTATIC CANCER

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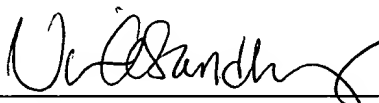
**Summary**

It is respectfully submitted that the pending claims 1, 3-13, 21, 23, 24, 33, 36, 37, 41-47, 49-56, 59-69, 72, 73, 75-81, and 90-101 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for  
Purdue Research Foundation

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**CERTIFICATE UNDER 37 CFR §1.10:**

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The undersigned hereby certifies that the Transmittal Letter and the paper(s) and/or fee(s), as described hereinabove, are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR §1.10 on the date indicated above and is addressed to Mail Stop Amendment, Assistant Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

By:   
Name: Sara Olson

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